Inflammatory Cytokine TNFalpha Promotes the Long-Term Expansion of Primary Hepatocytes in 3D Culture.

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Public Summary:
In the healthy adult liver, most hepatocytes proliferate minimally. However, upon physical or chemical injury to the liver, hepatocytes proliferate extensively in vivo under the direction of multiple extracellular cues, including Wnt and pro-inflammatory signals. Currently, liver organoids can be generated readily in vitro from bile-duct epithelial cells, but not hepatocytes. Here, we show that TNFalpha, an injury-induced inflammatory cytokine, promotes the expansion of hepatocytes in 3D culture and enables serial passaging and long-term culture for more than 6 months. Single-cell RNA sequencing reveals broad expression of hepatocyte markers. Strikingly, in vitro-expanded hepatocytes engrafted, and significantly repopulated, the injured livers of Fah(-/-) mice. We anticipate that tissue repair signals can be harnessed to promote the expansion of otherwise hard-to-culture cell-types, with broad implications.

Scientific Abstract:
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